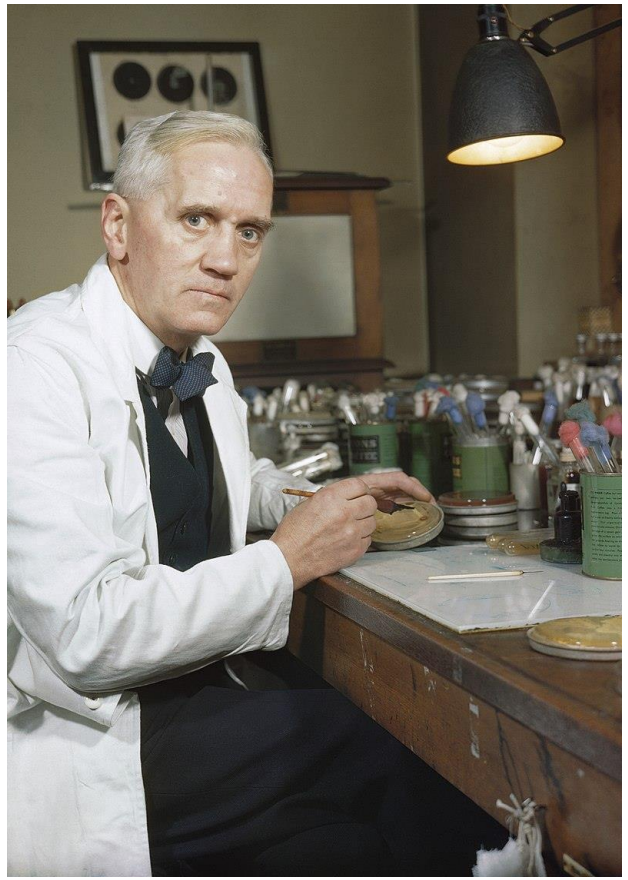
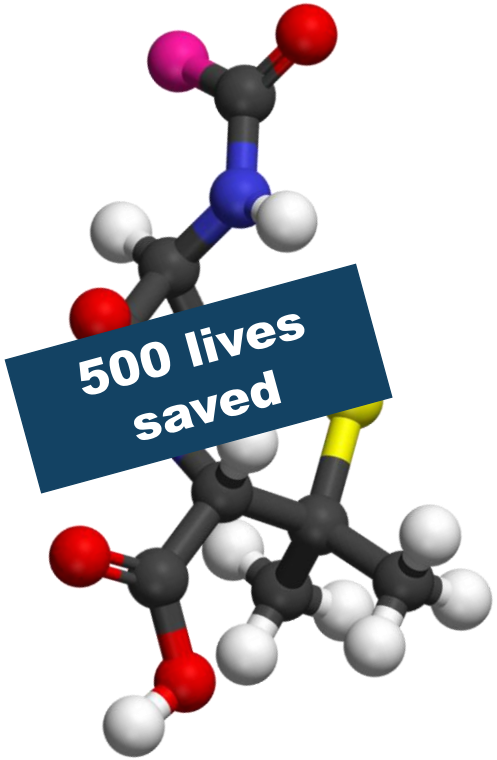
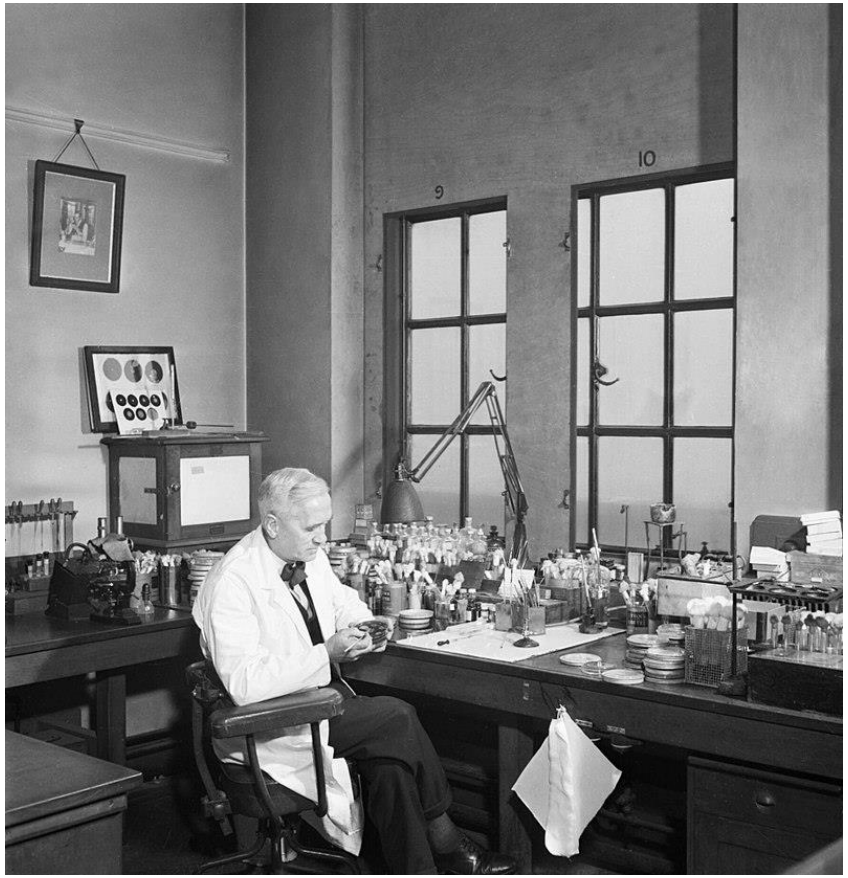






Sir Alexander Fleming

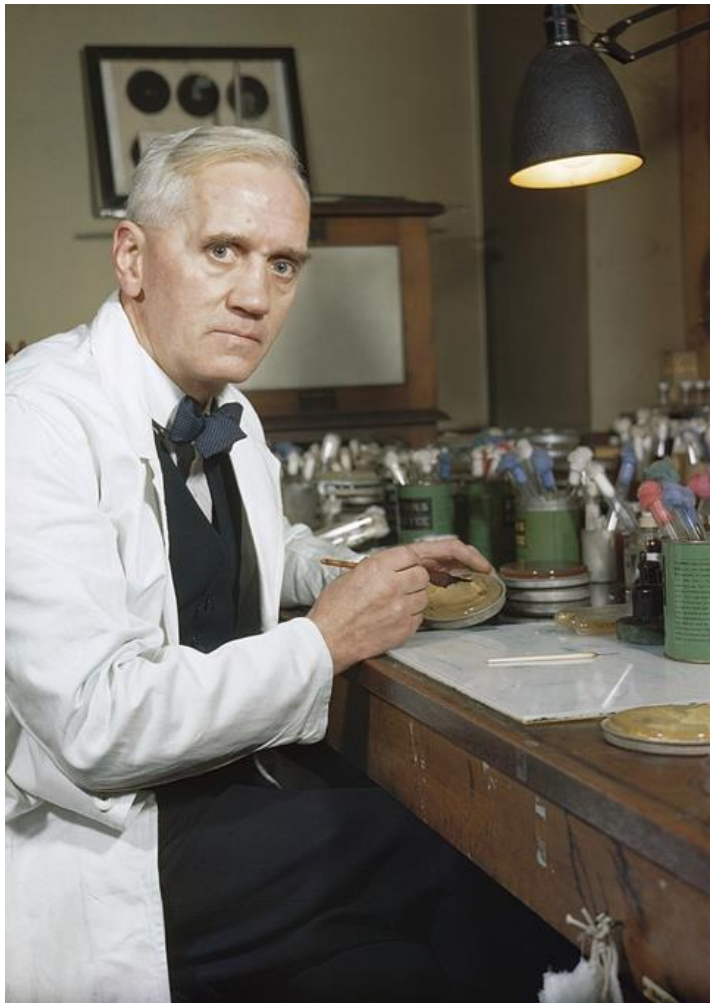
Best known for discovering the world's first broadly effective antibiotic substance, which he named penicillin.

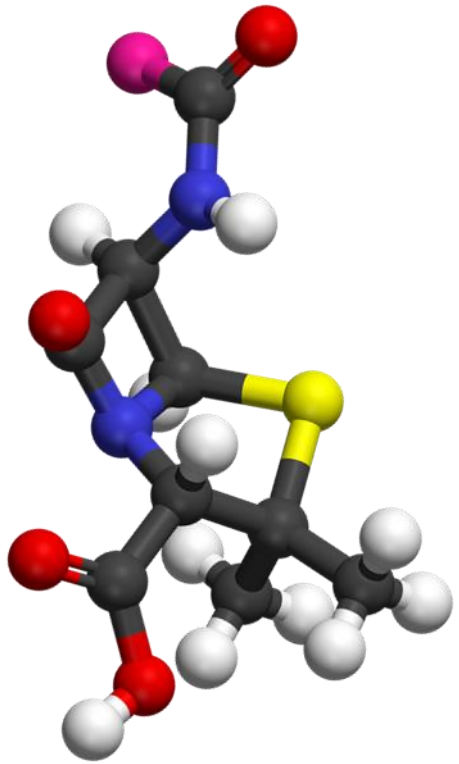
Anders Dernback text Wikipedia

Sir Alexander Fleming

One sometimes finds what one is not looking for. When I woke up just after dawn on September 28, 1928, I certainly didn't plan to revolutionize all medicine by discovering the world's first antibiotic, or bacteria killer. But I suppose that was exactly what I did.

—Alexander Fleming

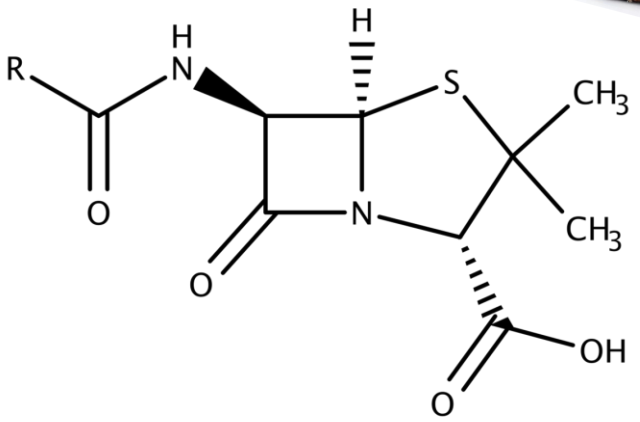




Sir Alexander Fleming

The development of the first antibiotic, penicillin, ranks among the top medical discoveries of all time, and was the subject of a Nobel Prize in 1945.

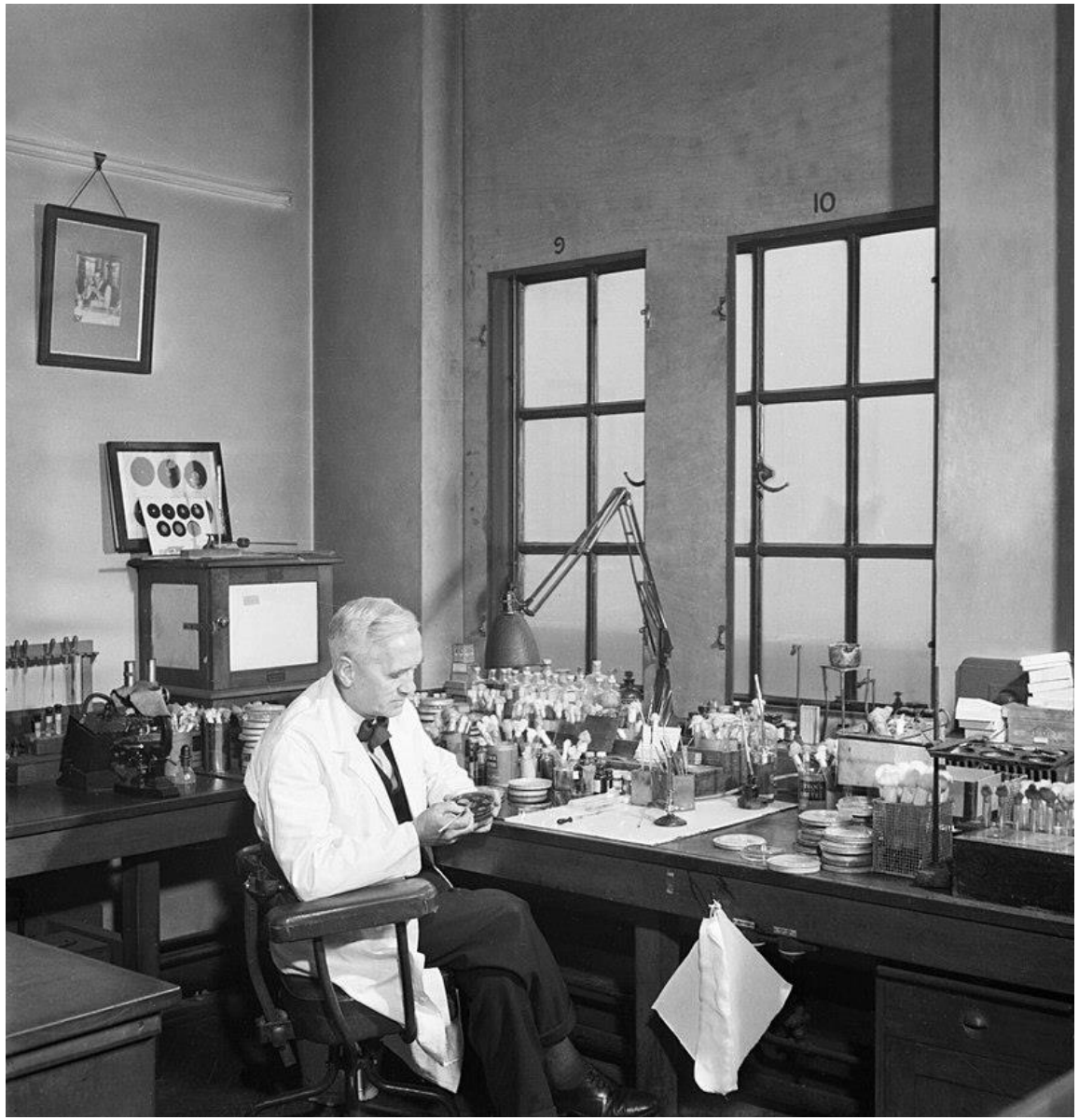
Although he initially improved, supplies of penicillin ran out and he succumbed to his infection. The dedicated work of the team of Florey, Chain and Heatley ushered in the age of modern medicine, and paved the way for drug discovery. It has been estimated that over 500 million lives have now been saved by penicillin.



Sir Alexander Fleming

Sir Alexander Fleming (centre) receiving the Nobel prize from King Gustaf V of Sweden (right) in 1945

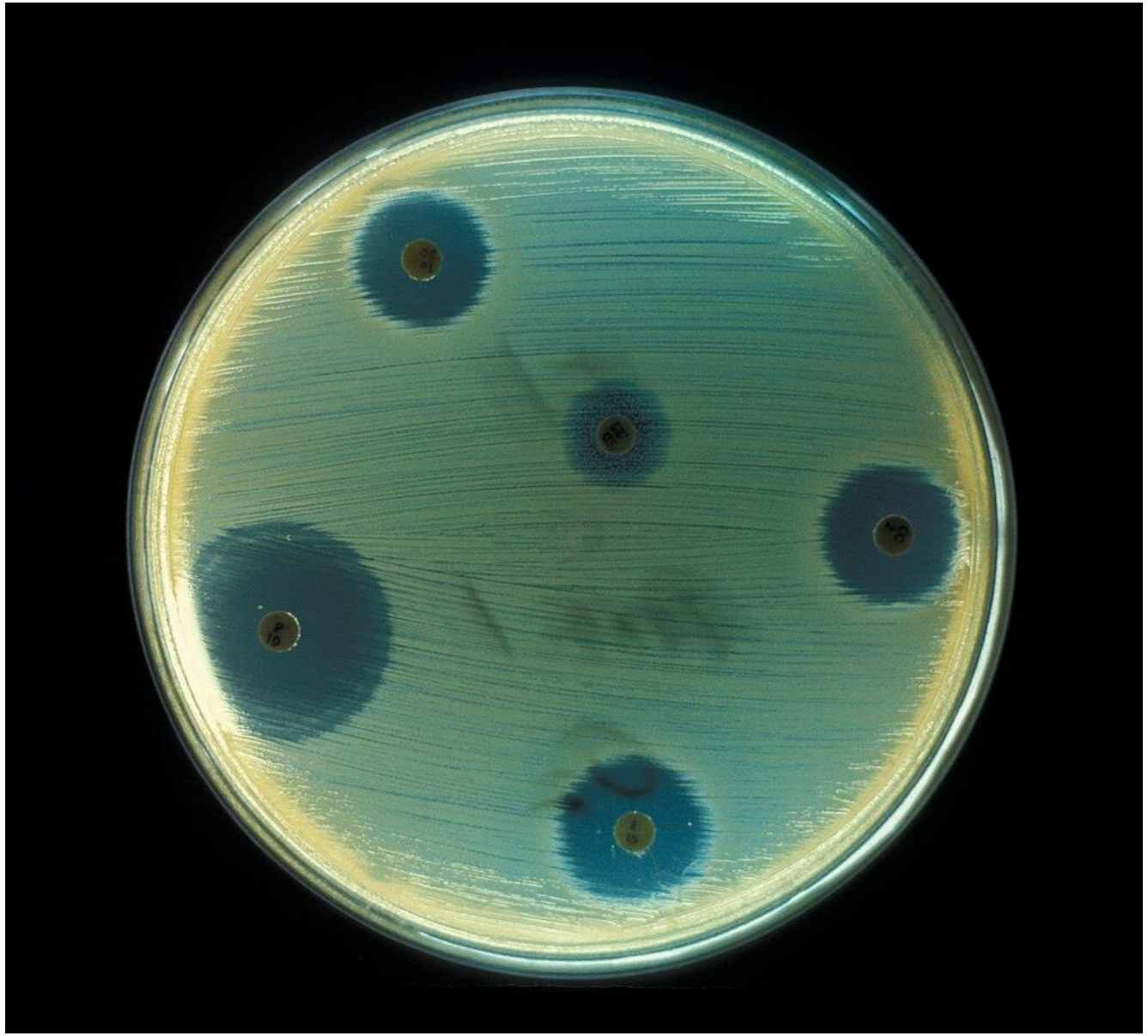
Sir Alexander Fleming



Sir Alexander Fleming (6 August 1881 – 11 March 1955) was a Scottish physician and microbiologist, best known for discovering the world's first broadly effective antibiotic substance, which he named penicillin. His discovery in 1928 of what was later named benzylpenicillin (or penicillin G) from the mould Penicillium rubens has been described as the "single greatest victory ever achieved over disease". For this discovery, he shared the Nobel Prize in Physiology or Medicine in 1945 with Howard Florey and Ernst Chain.

He also discovered the enzyme lysozyme from his nasal discharge in 1922, and along with it a bacterium he named Micrococcus lysodeikticus, later renamed Micrococcus luteus.

Sir Alexander Fleming



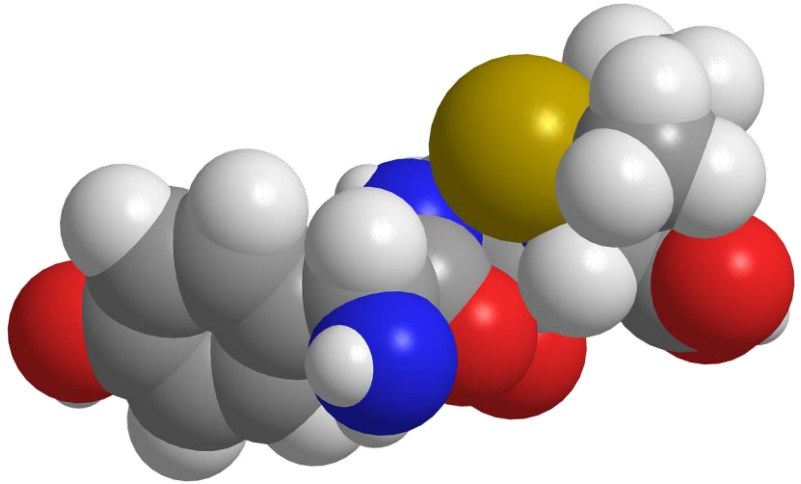
Modern antibiotics are tested using a method similar to Fleming's discovery.

Fleming was knighted for his scientific achievements in 1944. In 1999, he was named in Time magazine's list of the 100 Most Important People of the 20th century. In 2002, he was chosen in the BBC's television poll for determining the 100 Greatest Britons, and in 2009, he was also voted third "greatest Scot" in an opinion poll conducted by STV, behind only Robert Burns and William Wallace.

Sir Alexander Fleming

Early life and education

Born on 6 August 1881 at Lochfield farm near Darvel, in Ayrshire, Scotland, Alexander Fleming was the third of four children of farmer Hugh Fleming and Grace Stirling Morton, the daughter of a neighbouring farmer. Hugh Fleming had four surviving children from his first marriage. He was 59 at the time of his second marriage to Grace, and died when Alexander was seven.



Fleming went to Loudoun Moor School and Darvel School, and earned a two-year scholarship to Kilmarnock Academy before moving to London, where he attended the Royal Polytechnic Institution

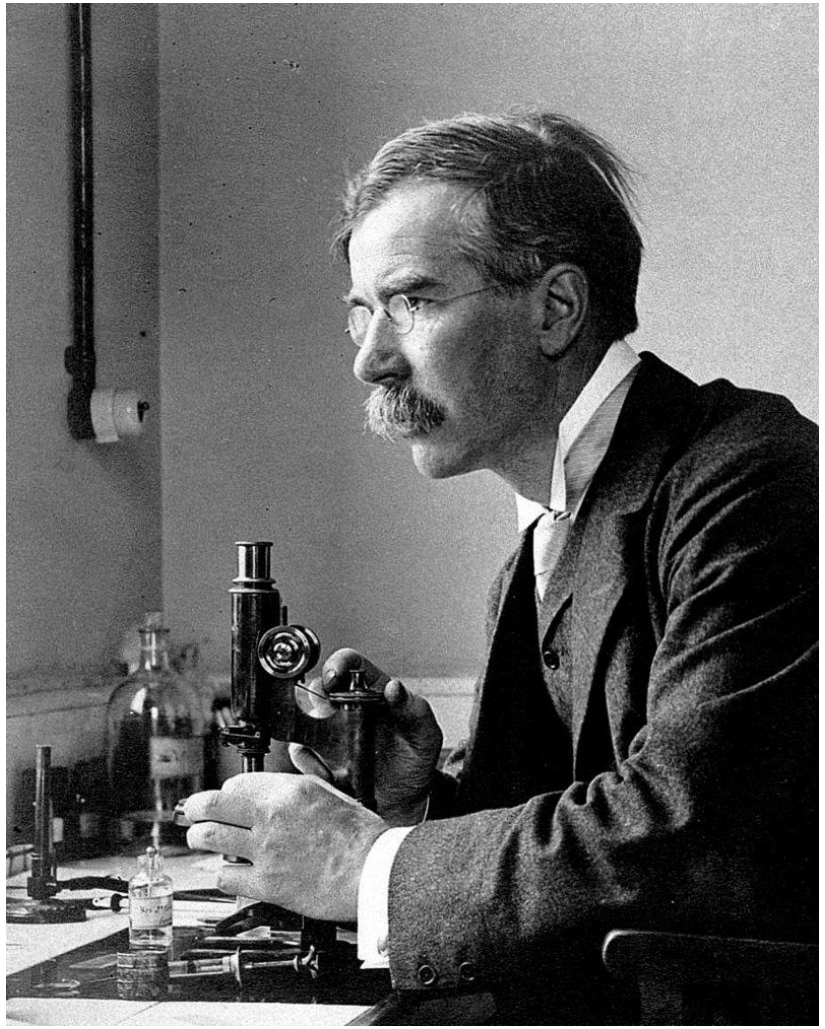
After working in a shipping office for four years, the twenty-year-old Alexander Fleming inherited some money from an uncle, John Fleming. His elder brother, Tom, was already a physician and suggested to him that he should follow the same career, and so in 1903, the younger Alexander enrolled at St Mary's Hospital Medical School in Paddington (now part of Imperial College London); he qualified with an MBBS degree from the school with distinction in 1906.

Sir Alexander Fleming

Fleming, who was a private in the London Scottish Regiment of the Volunteer Force from 1900 to 1914, had been a member of the rifle club at the medical school. The captain of the club, wishing to retain Fleming in the team, suggested that he join the research department at St Mary's, where he became assistant bacteriologist to Sir Almroth Wright, a pioneer in vaccine therapy and immunology. In 1908, he gained a BSc degree with gold medal in bacteriology, and became a lecturer at St Mary's until 1914.

Commissioned lieutenant in 1914 and promoted captain in 1917, Fleming served throughout World War I in the Royal Army Medical Corps, and was Mentioned in Dispatches. He and many of his colleagues worked in battlefield hospitals at the Western Front in France.

In 1918 he returned to St Mary's Hospital, where he was elected Professor of Bacteriology of the University of London in 1928. In 1951 he was elected the Rector of the University of Edinburgh for a term of three years



Almroth Wright

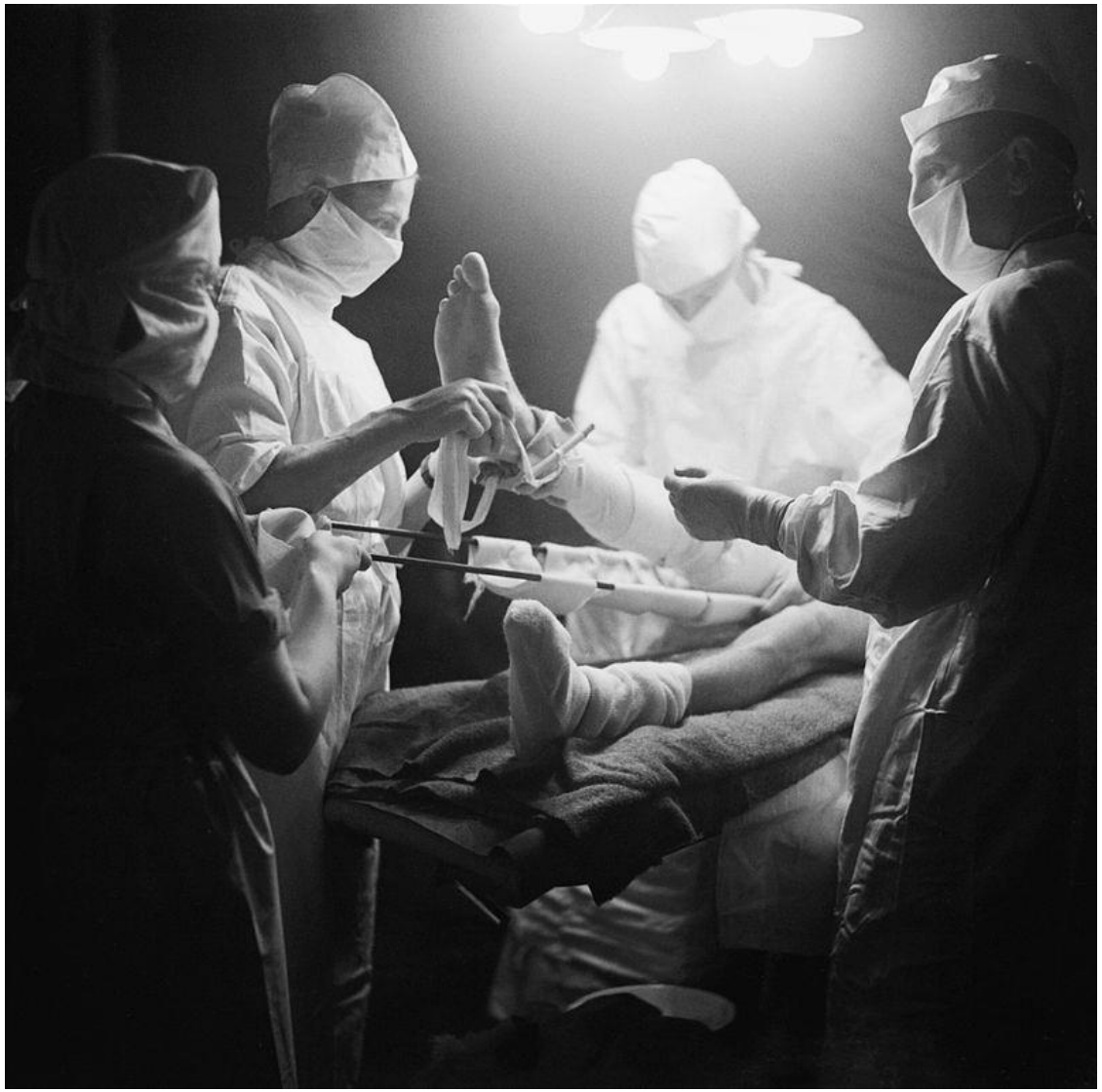
Sir Alexander Fleming

The London Scottish was a reserve infantry regiment then a company of the British Army. In its final incarnation it was A (The London Scottish) Company, the London Regiment until, on 1 May 2022, soldiers in the company transferred to foot guards regiments and the company became G (Messines) Company, Scots Guards, 1st Battalion London Guards.

Sir Alexander Fleming

The Royal Army Medical Corps (RAMC) was a specialist corps in the British Army which provided medical services to all Army personnel and their families, in war and in peace.

On 15 November 2024, the corps was amalgamated with the Royal Army Dental Corps and Queen Alexandra's Royal Army Nursing Corps to form the Royal Army Medical Service.



Sir Alexander Fleming

St Mary's Hospital is an NHS district general hospital in Paddington, in the City of Westminster, London, founded in 1845. Since the UK's first academic health science centre was created in 2008, it has been operated by Imperial College Healthcare NHS Trust, which also operates Charing Cross Hospital, Hammersmith Hospital, Queen Charlotte's and Chelsea Hospital and the Western Eye Hospital.

Until 1988 the hospital ran St Mary's Hospital Medical School, part of the federal University of London. In 1988 it merged with Imperial College London, and then with Charing Cross and Westminster Medical School in 1997 to form Imperial College School of Medicine. In 2007 Imperial College became an independent institution when it withdrew from the University of London.

Sir Alexander Fleming

St Mary´s Hospital London UK y 2017

Sir Alexander Fleming

The original block in Norfolk Place

Sir Alexander Fleming

Antiseptics

During World War I, Fleming with Leonard Colebrook and Sir Almroth Wright joined the war efforts and practically moved the entire Inoculation Department of St Mary's to the British military hospital at Boulogne-sur-Mer. Serving as a temporary lieutenant of the Royal Army Medical Corps, he witnessed the death of many soldiers from sepsis resulting from infected wounds. Antiseptics, which were used at the time to treat infected wounds, he observed, often worsened the injuries.

In an article published in the medical journal The Lancet in 1917, he described an ingenious experiment, which he was able to conduct as a result of his own glassblowing skills, in which he explained why antiseptics were killing more soldiers than infection itself during the war. Antiseptics worked well on the surface, but deep wounds tended to shelter anaerobic bacteria from the antiseptic agent, and antiseptics seemed to remove beneficial agents produced that protected the patients in these cases at least as well as they removed bacteria, and did nothing to remove the bacteria that were out of reach. Wright strongly supported Fleming's findings, but despite this, most army physicians over the course of the war continued to use antiseptics even in cases where this worsened the condition of the patients.

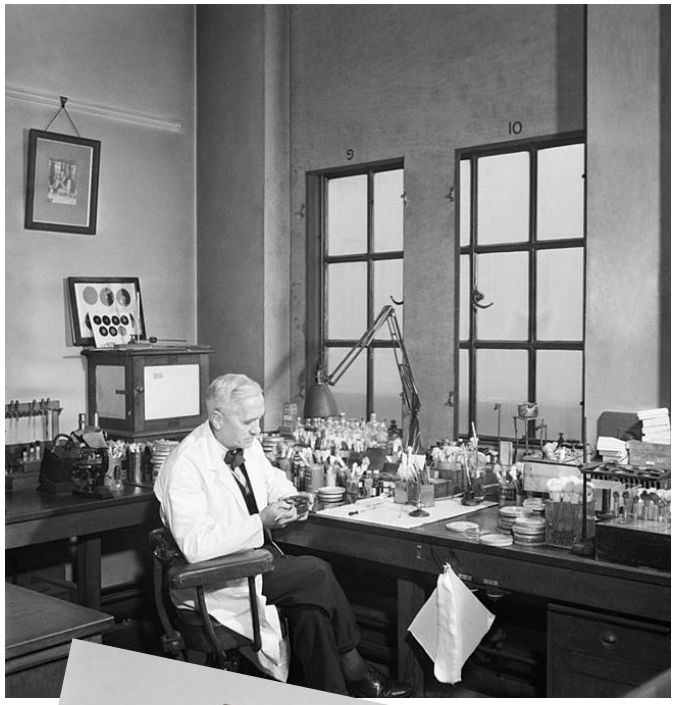
Discovery of lysozyme

At St Mary's Hospital, Fleming continued his investigations into bacteria culture and antibacterial substances. As his research scholar at the time V. D. Allison recalled, Fleming was not a tidy researcher and usually expected unusual bacterial growths in his culture plates

Sir Alexander Fleming

Fleming had teased Allison of his "excessive tidiness in the laboratory", and Allison rightly attributed such untidiness as the success of Fleming's experiments, and said, "[If] he had been as tidy as he thought I was, he would not have made his two great discoveries."

In late 1921, while Fleming was maintaining agar plates for bacteria, he found that one of the plates was contaminated with bacteria from the air. When he added nasal mucus, he found that the mucus inhibited the bacterial growth. Surrounding the mucus area was a clear transparent circle (1 cm from the mucus), indicating the killing zone of bacteria, followed by a glassy and translucent ring beyond which was an opaque area indicating normal bacterial growth. In the next test, he used bacteria maintained in saline that formed a yellow suspension. Within two minutes of adding fresh mucus, the yellow saline turned completely clear. He extended his tests using tears, which were contributed by his co-workers. As Allison reminisced, saying, "For the next five or six weeks, our tears were the source of supply for this extraordinary phenomenon. Many were the lemons we used (after the failure of onions) to produce a flow of tears... The demand by us for tears was so great, that laboratory attendants were pressed into service, receiving threepence for each contribution.



Sir Alexander Fleming

His further tests with sputum, cartilage, blood, semen, ovarian cyst fluid, pus, and egg white showed that the bactericidal agent was present in all of these. He reported his discovery before the Medical Research Club in December and before the Royal Society the next year but failed to stir any interest, as Allison recollected:

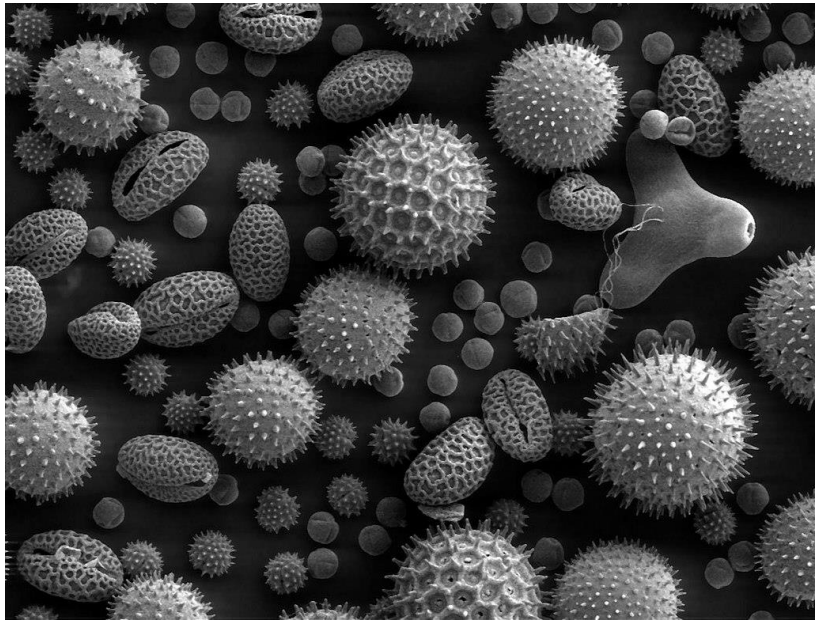
I was present at this [Medical Research Club] meeting as Fleming's guest. His paper describing his discovery was received with no questions asked and no discussion, which was most unusual and an indication that it was considered to be of no importance. The following year he read a paper on the subject before the Royal Society, Burlington House, Piccadilly and he and I gave a demonstration of our work. Again with one exception little comment or attention was paid to it.

Sir Alexander Fleming

Reporting in the 1 May 1922 issue of the Proceedings of the Royal Society B: Biological Sciences under the title "On a remarkable bacteriolytic element found in tissues and secretions", Fleming wrote:

In this communication I wish to draw attention to a substance present in the tissues and secretions of the body, which is capable of rapidly dissolving certain bacteria. As this substance has properties akin to those of ferments I have called it a "Lysozyme", and shall refer to it by this name throughout the communication. The lysozyme was first noticed during some investigations made on a patient suffering from acute coryza.

Rhinitis, also known as coryza, is irritation and inflammation of the mucous membrane inside the nose. Common symptoms are a stuffy nose, runny nose, sneezing, and post-nasal drip.
The inflammation is caused by viruses, bacteria, irritants or allergens. The most common kind of rhinitis is allergic rhinitis, which is usually triggered by airborne allergens such as pollen and dander. Rhinitis is categorized into three types (although infectious rhinitis is typically regarded as a separate clinical entity due to its transient nature)



Sir Alexander Fleming

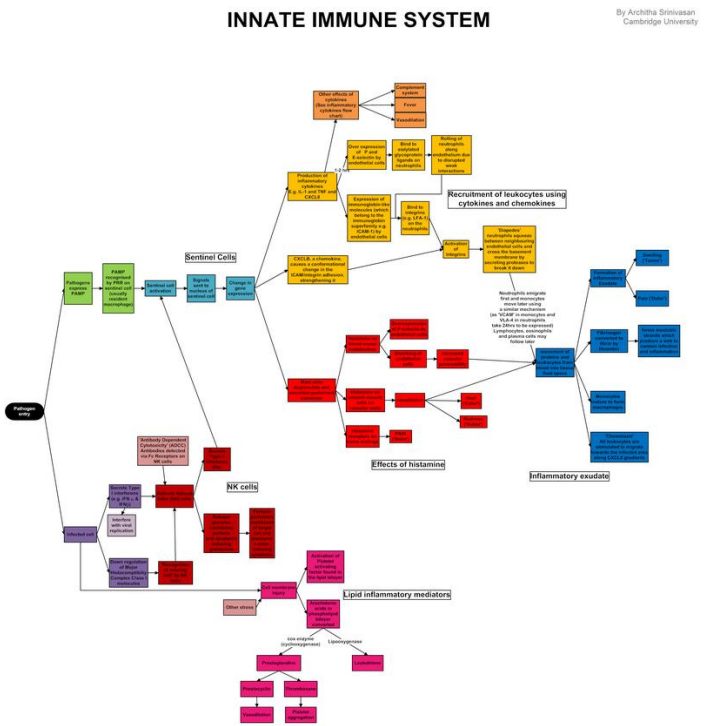
This was the first recorded discovery of lysozyme. With Allison, he published further studies on lysozyme in October issue of the British Journal of Experimental Pathology the same year. Although he was able to obtain larger amounts of lysozyme from egg whites, the enzyme was only effective against small counts of harmless bacteria, and therefore had little therapeutic potential. This indicates one of the major differences between pathogenic and harmless bacteria. Described in the original publication, "a patient suffering from acute coryza" was later identified as Fleming himself. His research notebook dated 21 November 1921 showed a sketch of the culture plate with a small note: "Staphyloid coccus from A.F.'s nose." He also identified the bacterium present in the nasal mucus as Micrococcus Lysodeikticus, giving the species name (meaning "lysis indicator" for its susceptibility to lysozymal activity). The species was reassigned as Micrococcus luteus in 1972. The "Fleming strain" (NCTC2665) of this bacterium has become a model in different biological studies. The importance of lysozyme was not recognised, and Fleming was well aware of this, in his presidential address at the Royal Society of Medicine meeting on 18 October 1932

he said:

I choose lysozyme as the subject for this address for two reasons, firstly because I have a fatherly interest in the name, and, secondly, because its importance in connection with natural immunity does not seem to be generally appreciated

Sir Alexander Fleming

In his Nobel lecture on 11 December 1945, he briefly mentioned lysozyme, saying, "Penicillin was not the first antibiotic I happened to discover." It was only towards the end of the 20th century that the true importance of Fleming's discovery in immunology was realised as lysozyme became the first antimicrobial protein discovered that constitute part of our innate immunity.



The innate immune system or nonspecific immune system is one of the two main immunity strategies in vertebrates (the other being the adaptive immune system). The innate immune system is an alternate defense strategy and is the dominant immune system response found in plants, fungi, prokaryotes, and invertebrates.
The major functions of the innate immune system are to:

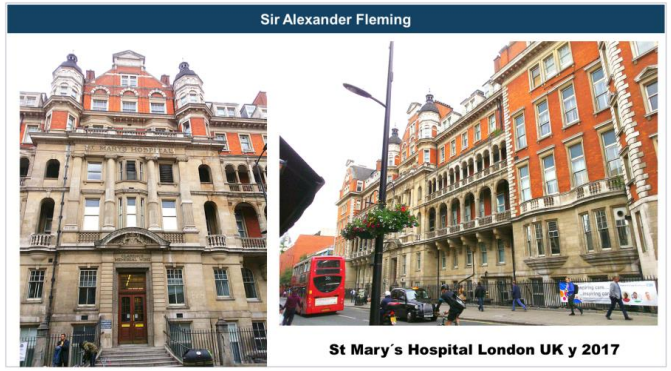
recruit immune cells to infection sites by producing chemical factors, including chemical mediators called cytokines
activate the complement cascade to identify bacteria, activate cells, and promote clearance of antibody complexes or dead cells
identify and remove foreign substances present in organs, tissues, blood and lymph, by specialized white blood cells
activate the adaptive immune system through antigen presentation
act as a physical and chemical barrier to infectious agents; via physical measures such as skin and mucus, and chemical measures such as clotting factors and host defence peptides.

Discovery of penicillin

Sir Alexander Fleming

The history of penicillin follows observations and discoveries of evidence of antibiotic activity of the mould Penicillium that led to the development of penicillins that became the first widely used antibiotics. Following the production of a relatively pure compound in 1942, penicillin was the first naturally-derived antibiotic.

Ancient societies used moulds to treat infections, and in the following centuries many people observed the inhibition of bacterial growth by moulds. While working at St Mary's Hospital in London in 1928, Scottish physician Alexander Fleming was the first to experimentally determine that a Penicillium mould secretes an antibacterial substance, which he named "penicillin". The mould was found to be a variant of Penicillium notatum (now called Penicillium rubens), a contaminant of a bacterial culture in his laboratory. The work on penicillin at St Mary's ended in 1929.



Sir Alexander Fleming

In 1939, a team of scientists at the Sir William Dunn School of Pathology at the University of Oxford, led by Howard Florey that included Edward Abraham, Ernst Chain, Mary Ethel Florey, Norman Heatley and Margaret Jennings, began researching penicillin. They developed a method for cultivating the mould and extracting, purifying and storing penicillin from it, together with an assay for measuring its purity. They carried out experiments on animals to determine penicillin's safety and effectiveness before conducting clinical trials and field tests. They derived penicillin's chemical structure and determined how it works. The private sector and the United States Department of Agriculture located and produced new strains and developed mass production techniques. During the Second World War penicillin became an important part of the Allied war effort, saving thousands of lives. Alexander Fleming, Howard Florey and Ernst Chain shared the 1945 Nobel Prize in Physiology or Medicine for the discovery and development of penicillin.

After the end of the war in 1945, penicillin became widely available. Dorothy Hodgkin determined its chemical structure, for which she received the Nobel Prize in Chemistry in 1964. This led to the development of semisynthetic penicillins that were more potent and effective against a wider range of bacteria. The drug was synthesised in 1957, but cultivation of mould remains the primary means of production. It was discovered that adding penicillin to animal feed increased weight gain, improved feed-conversion efficiency, promoted more uniform growth and facilitated disease control. Agriculture became a major user of penicillin. Shortly after their discovery of penicillin, the Oxford team reported penicillin resistance in many bacteria. Research that aims to circumvent and understand the mechanisms of antibiotic resistance continues today.

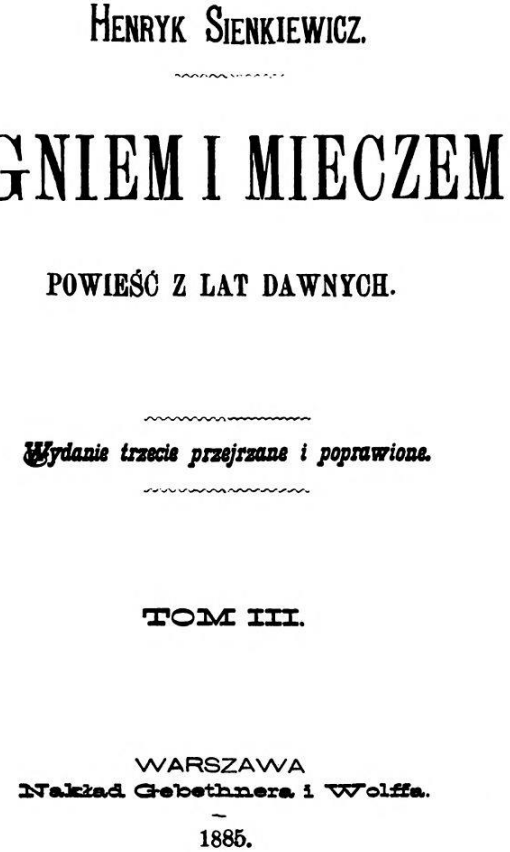
Sir Alexander Fleming

Many ancient cultures, including those in Australia, China, Egypt, Greece and India, independently discovered the useful properties of fungi and plants in treating infections. These treatments often worked because many organisms, including many species of mould, naturally produce antibiotics. However, ancient practitioners could not precisely identify or isolate the active components in these organisms.

In England in 1640, the idea of using mould as a form of medical treatment was recorded by apothecaries such as the botanist John Parkinson, who documented the use of moulds to treat infections in his book on pharmacology. In 17th-century Poland, wet bread was mixed with spider webs (which often contained fungal spores) to treat wounds. The technique was mentioned by Henryk Sienkiewicz in his 1884 novel With Fire and Sword.

John Parkinson (1567–1650; buried 6 August 1650) was the last of the great English herbalists and one of the first of the great English botanists. He was apothecary to James I and a founding member of the Worshipful Society of Apothecaries in December 1617, and was later Royal Botanist to Charles I. He is known for two monumental works, Paradisi in Sole Paradisus Terrestris (Park-in-Sun's Terrestrial Paradise, 1629), which generally describes the proper cultivation of plants; and Theatrum Botanicum (The Botanical Theatre or Theatre of Plants, 1640), the most complete and beautifully presented English treatise on plants of its time.

Sir Alexander Fleming



HENRYK SIENKIEWICZ.

OGNIEM I MIECZEM

POWIEŚĆ Z LAT DAWNYCH.

Wydanie trzecie przejrzane i poprawione.

TOM III.

WARSZAWA
Nakład Gebethnera i Wolffa.
1885.

By Fire and Sword (Polish: Ogniem i mieczem) is a historical novel by the Polish author Henryk Sienkiewicz, published in 1884. It is the first volume of a series known to Poles as The Trilogy, followed by The Deluge (Potop, 1886) and Fire in the Steppe (originally published under the Polish title Pan Wołodyjowski, which translates to Lord Wolodyjowski). The novel has been adapted as a film several times, most recently in 1999.

By Fire and Sword is a historical fiction novel, set in the 17th century in the Polish–Lithuanian Commonwealth during the Khmelnytsky Uprising.

Sir Alexander Fleming

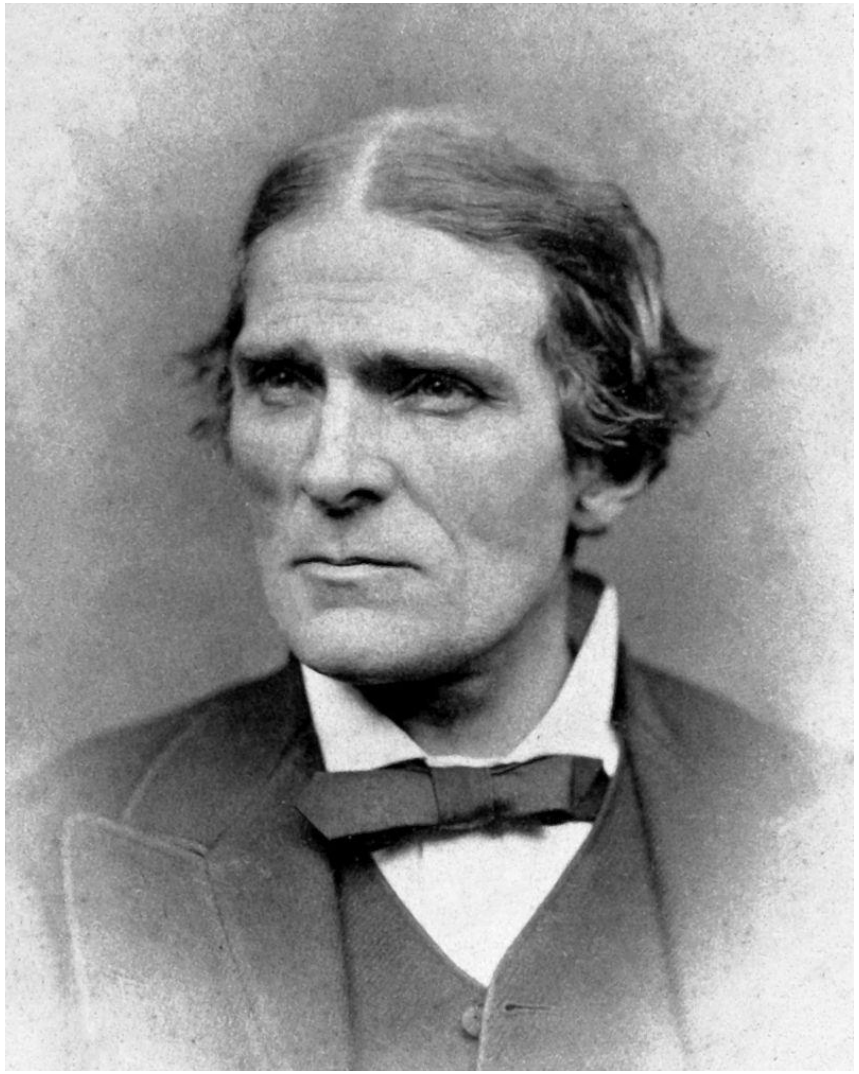
Henryk Adam Aleksander Pius; 5 May 1846 – 15 November 1916), also known by the pseudonym Litwos, was a Polish epic writer. He is remembered for his historical novels, such as the Trilogy series and especially for his internationally known best-seller Quo Vadis (1896).
Born into an impoverished Polish noble family in Russian-ruled Congress Poland, in the late 1860s he began publishing journalistic and literary pieces. In the late 1870s he traveled to the United States, sending back travel essays that won him popularity with Polish readers.

Many of his novels remain in print. In Poland he is known for his "Trilogy" of historical novels – With Fire and Sword, The Deluge, and Sir Michael – set in the 17th-century Polish–Lithuanian Commonwealth; internationally he is known for Quo Vadis, set in Nero's Rome. The Trilogy and Quo Vadis have been filmed, the latter several times, with Hollywood's 1951 version receiving the most international recognition.

Sir Alexander Fleming

Sir John Scott Burdon-Sanderson, 1st Baronet, FRS, HFRSE D.Sc. (21 December 1828 – 23 November 1905) was an English physiologist born near Newcastle upon Tyne, and a member of a well known Northumbrian family.

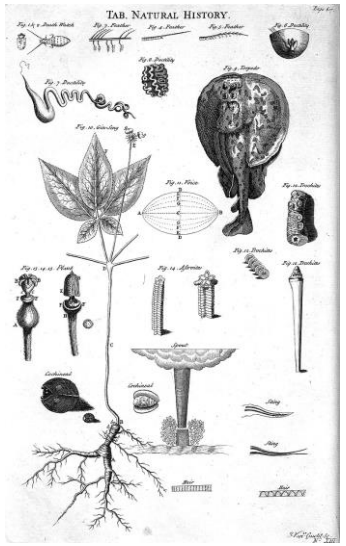
He reported that Penicillium inhibited the growth of bacteria, an observation which places him among the forerunners of Alexander Fleming.

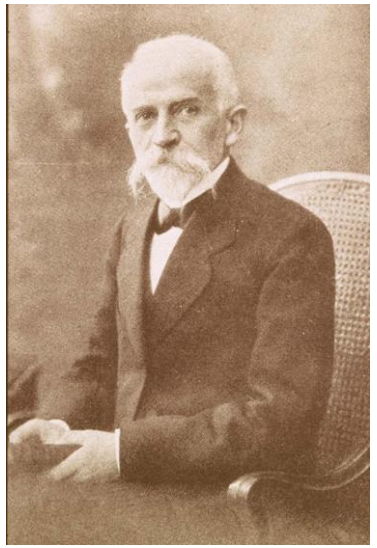


Sir Alexander Fleming

In 1871, Sir John Scott Burdon-Sanderson reported that culture fluid covered with mould would produce no bacterial growth. Joseph Lister, an English surgeon and the father of modern antisepsis, observed in November 1871 that urine samples contaminated with mould also did not permit the growth of bacteria. He also described the antibacterial action on human tissue of Penicillium glaucum but did not publish his results. In 1875 John Tyndall demonstrated to the Royal Society the antibacterial action of the Penicillium fungus.

In 1876, German biologist Robert Koch discovered that a bacterium (Bacillus anthracis) was the causative pathogen of anthrax, which became the first demonstration that a specific bacterium caused a specific disease and the first direct evidence of germ theory of diseases. In 1877, French biologists Louis Pasteur and Jules Francois Joubert observed that cultures of anthrax bacilli, when contaminated with other bacteria, could be successfully inhibited.





Sir Alexander Fleming

The phenomenon was described by Pasteur and Koch as antibacterial activity and was named antibiosis by French biologist Jean Paul Vuillemin in 1877. (The term antibiosis, meaning 'against life', was adopted as antibiotic by American biologist and later Nobel laureate Selman Waksman in 1947. However, Paul de Kruif's 1926 Microbe Hunters notes that Pasteur believed that this was contamination by other bacteria rather than by mould. In 1887, Swiss physician Carl Garré developed a test method using glass plate to see bacterial inhibition and found similar results. Using his gelatin-based culture plate, he grew two different species of bacteria and found that their growths were inhibited differently, as he reported:

I inoculated on the untouched cooled [gelatin] plate alternate parallel strokes of B. fluorescens [Pseudomonas fluorescens] and Staph. pyogenes [Streptococcus pyogenes]... B. fluorescens grew more quickly... [This] is not a question of overgrowth or crowding out of one by another quicker-growing species, as in a garden where luxuriantly growing weeds kill the delicate plants. Nor is it due to the utilization of the available foodstuff by the more quickly growing organisms, rather there is an antagonism caused by the secretion of specific, easily diffusible substances which are inhibitory to the growth of some species but completely ineffective against others.

Sir Alexander Fleming

Vincenzo Tiberio (May 1, 1869 – January 7, 1915) was an Italian researcher and medical officer of the Medical Corps of the Italian Navy and physician at the University of Naples. Observing that people complained of intestinal disorders after the walls of a well which supplied drinking water was cleaned off, he published a little noticed 1895 paper on the bactericidal effect of some molds, 35 years before Alexander Fleming's discovery of penicillin.

hich Tiberius confirmed through in vivo experimentation, both on guinea pigs and rabbits. The research done by Vincenzo Tiberio was a complete scientific cycle of experiments. Starting from observation, the proving of the initial hypothesis, and also the preparation of the antibiotic substance to show its effect in vitro and in vivo. He also managed to evaluate the effective doses and time of the antibiotic efficacy. In 1895 he published the results of his experiments in an Italian medical journal, but the work was disregarded as coincidence and received no further study.

Sir Alexander Fleming

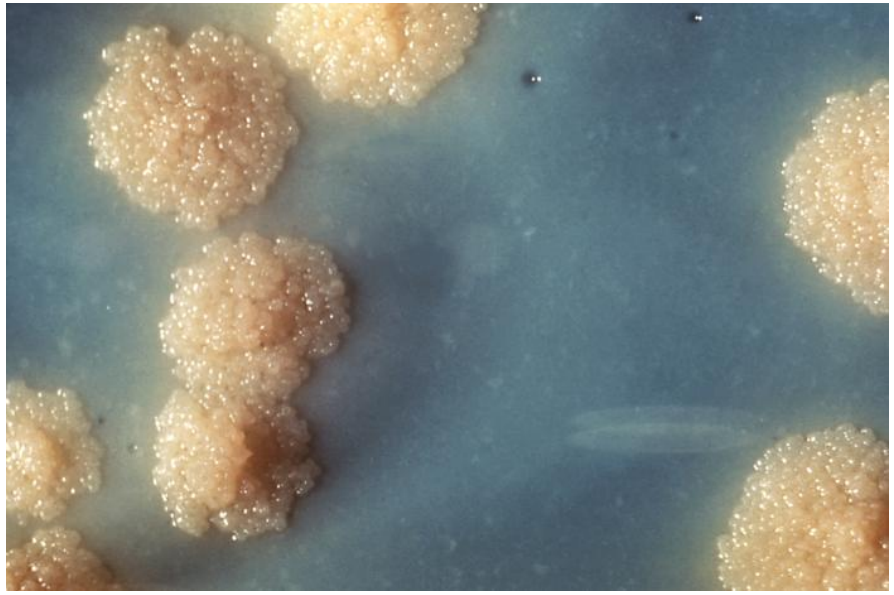
In 1895, Vincenzo Tiberio, an Italian physician at the University of Naples, published research on moulds initially found in a water well in Arzano; from his observations, he concluded that these moulds contained soluble substances having antibacterial action. Two years later, Ernest Duchesne at École du Service de Santé Militaire in Lyon independently discovered the healing properties of a P. glaucum mould, even curing infected guinea pigs of typhoid. He published his results in a dissertation in 1897.

Duchesne was using a discovery made earlier by Arab stable boys, who used moulds to cure sores on horses. He did not claim that the mould contained any antibacterial substance, only that the mould somehow protected the animals.

Penicillin does not cure typhoid and so it remains unknown which substance might have been responsible. A Pasteur Institute scientist, Costa Rican Clodomiro Picado Twight, similarly recorded the antibiotic effect of Penicillium in 1923. In these early stages of penicillin research, most species of Penicillium were non-specifically referred to as P. glaucum, so that it is impossible to know the exact species and that it was really penicillin that prevented bacterial grow

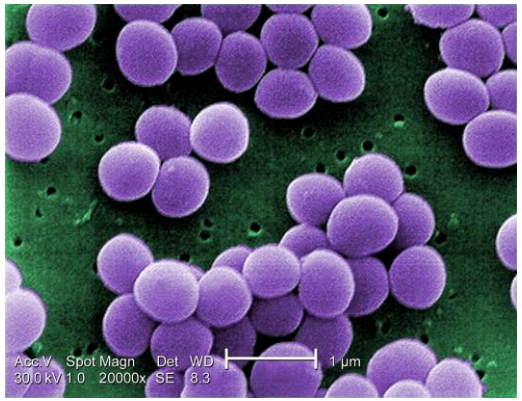
Sir Alexander Fleming

Andre Gratia and Sara Dath at the Free University of Brussels studied the effects of mould samples on bacteria. In 1924, they found that dead Staphylococcus aureus cultures were contaminated by a mould, a streptomycete. Upon further experimentation, they showed that the mould extract could kill not only S. aureus, but also Pseudomonas aeruginosa, Mycobacterium tuberculosis and Escherichia coli. Gratia called the antibacterial agent "mycolysate". The next year they found another killer mould that could inhibit B. anthracis. Reporting in Comptes rendus des séances de la Société de Biologie et de ses filiales, they identified the mould as P. glaucum. But these findings received little attention as the antibacterial agent and its medical value were not fully understood, and Gratia's samples were lost



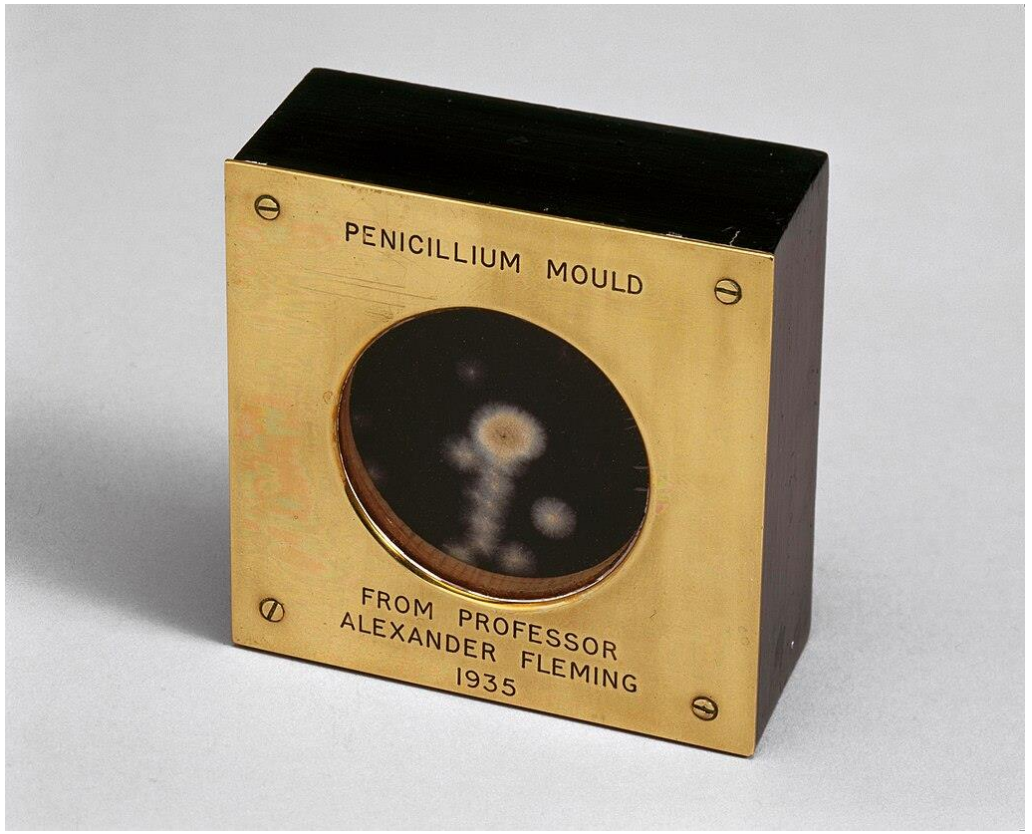
This is a close-up of a Mycobacterium tuberculosis culture revealing this organism's colonial morphology. Note the colorless rough surface, which are typical morphologic characteristics seen in Mycobacterium tuberculosis colonial growth. Macroscopic examination of colonial growth patterns is still one of the ways microorganisms are often identified.

Under a very high magnification of 20,000x, this scanning electron micrograph (SEM) shows a strain of Staphylococcus aureus bacteria taken from a vancomycin intermediate resistant culture (VISA).



Sir Alexander Fleming

St Mary's Hospital showing Fleming's lab and Praed Street



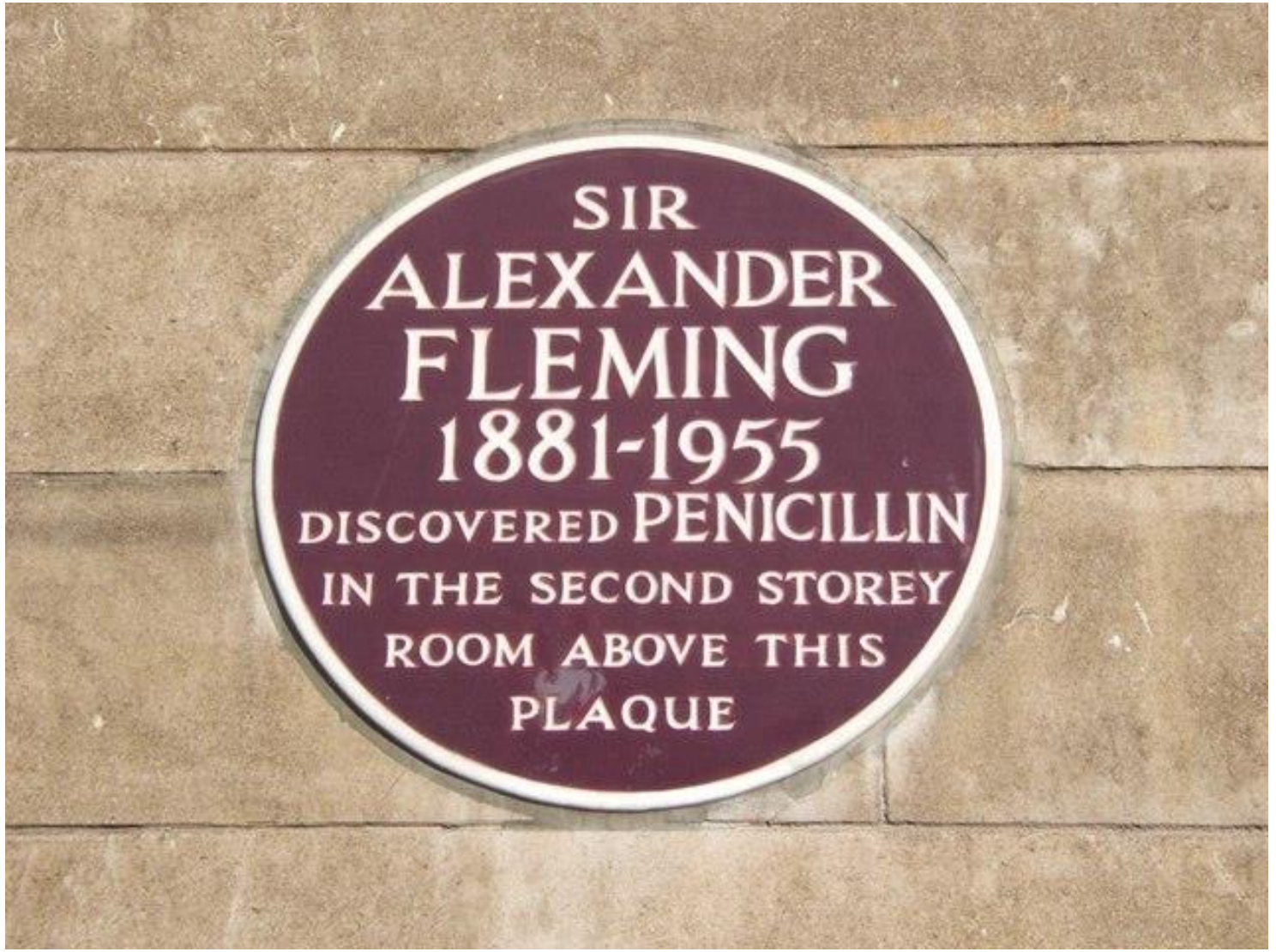
Sample of penicillin mould presented by Alexander Fleming to Douglas Macleod in 1935

Sir Alexander Fleming

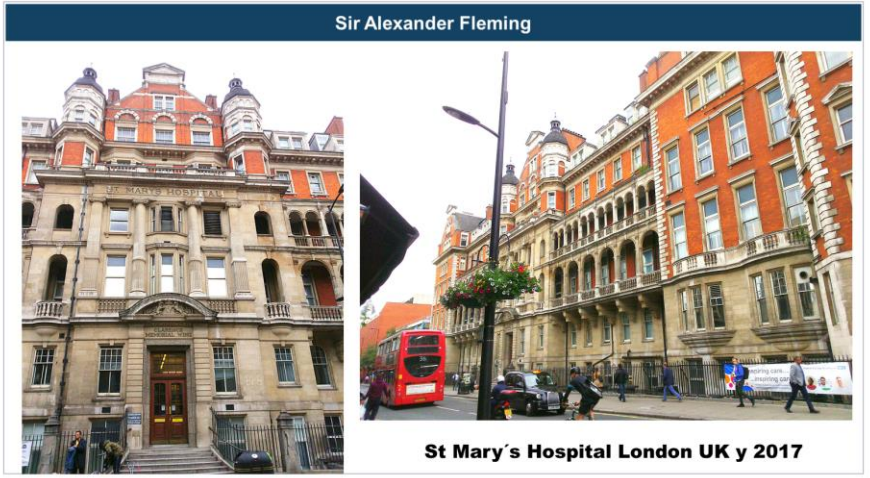
By 1927, Fleming had been investigating the properties of staphylococci. He was already well known from his earlier work, and had developed a reputation as a brilliant researcher. In 1928, he studied the variation of Staphylococcus aureus grown under natural condition, after the work of Joseph Warwick Bigger, who discovered that the bacterium could grow into a variety of types (strains). On 3 September 1928, Fleming returned to his laboratory having spent a holiday with his family at Suffolk. Before leaving for his holiday, he inoculated staphylococci on culture plates and left them on a bench in a corner of his laboratory.
On his return, Fleming noticed that one culture was contaminated with a fungus, and that the colonies of staphylococci immediately surrounding the fungus had been destroyed, whereas other staphylococci colonies farther away were normal, famously remarking "That's funny"Fleming showed the contaminated culture to his former assistant Merlin Pryce, who reminded him, "That's how you discovered lysozyme

He identified the mould as being from the genus Penicillium. He suspected it to be P. chrysogenum, but a colleague Charles J. La Touche identified it as P. rubrum. (It was later corrected as P. notatum and then officially accepted as P. chrysogenum; in 2011, it was resolved as P. rubens.)

Sir Alexander Fleming



The laboratory in which Fleming discovered and tested penicillin is preserved as the Alexander Fleming Laboratory Museum in St. Mary's Hospital, Paddington. The source of the fungal contaminant was established in 1966 as coming from La Touche's room, which was directly below Fleming's.



Sir Alexander Fleming

Fleming grew the mould in a pure culture and found that the culture broth contained an antibacterial substance. He investigated its anti-bacterial effect on many organisms, and noticed that it affected bacteria such as staphylococci and many other Gram-positive pathogens that cause scarlet fever, pneumonia, meningitis and diphtheria, but not typhoid fever or paratyphoid fever, which are caused by Gram-negative bacteria, for which he was seeking a cure at the time. It also affected Neisseria gonorrhoeae, which causes gonorrhoea, although this bacterium is Gram-negative. After some months of calling it "mould juice" or "the inhibitor", he gave the name penicillin on 7 March 1929 for the antibacterial substance present in the mould.

Reception and publication

Fleming presented his discovery on 13 February 1929 before the Medical Research Club. His talk on "A medium for the isolation of Pfeiffer's bacillus" did not receive any particular attention or comment. Henry Dale, the then Director of National Institute for Medical Research and chair of the meeting, much later reminisced that he did not even sense any striking point of importance in Fleming's speech. Fleming published his discovery in 1929 in the British Journal of Experimental Pathology, but little attention was paid to the article. His problem was the difficulty of producing penicillin in large amounts, and moreover, isolation of the main compound. Even with the help of Harold Raistrick and his team of biochemists at the London School of Hygiene & Tropical Medicine, chemical purification was futile. "As a result, penicillin languished largely forgotten in the 1930s", as Milton Wainwright described.

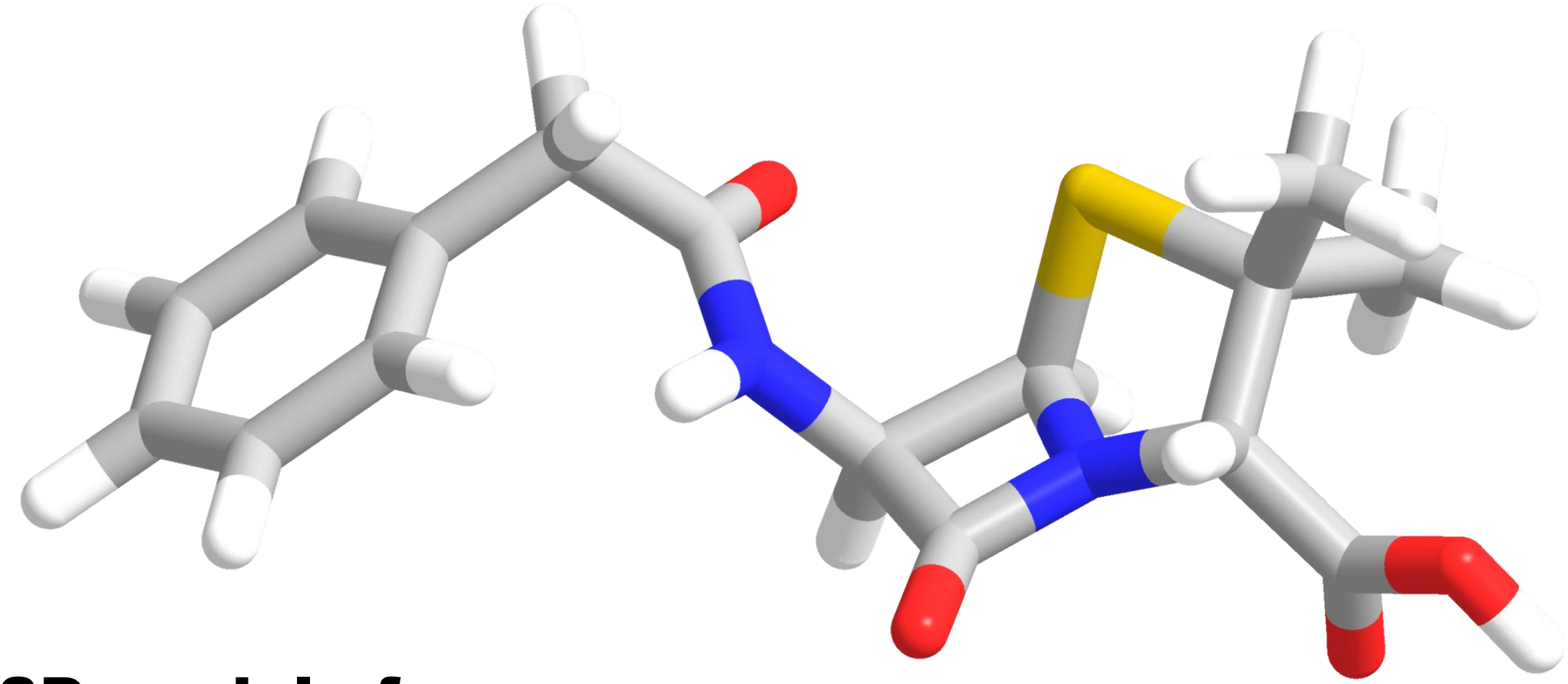
Sir Alexander Fleming

As late as in 1936, there was no appreciation for penicillin. When Fleming talked of its medical importance at the Second International Congress of Microbiology held in London, no one believed him. As Allison, his companion in both the Medical Research Club and international congress meeting, remarked the two occasions:

[Fleming at the Medical Research Club meeting] suggested the possible value of penicillin for the treatment of infection in man. Again there was a total lack of interest and no discussion. Fleming was keenly disappointed, but worse was to follow. He read a paper on his work on penicillin at a meeting of the International Congress of Microbiology, attended by the foremost bacteriologists from all over the world. There was no support for his views on its possible future value for the prevention and treatment of human infections and discussion was minimal. Fleming bore these disappointments stoically, but they did not alter his views or deter him from continuing his investigation of penicillin.

In 1941, the British Medical Journal reported that "[Penicillin] does not appear to have been considered as possibly useful from any other point of view.

Sir Alexander Fleming



3D-model of benzylpenicillin

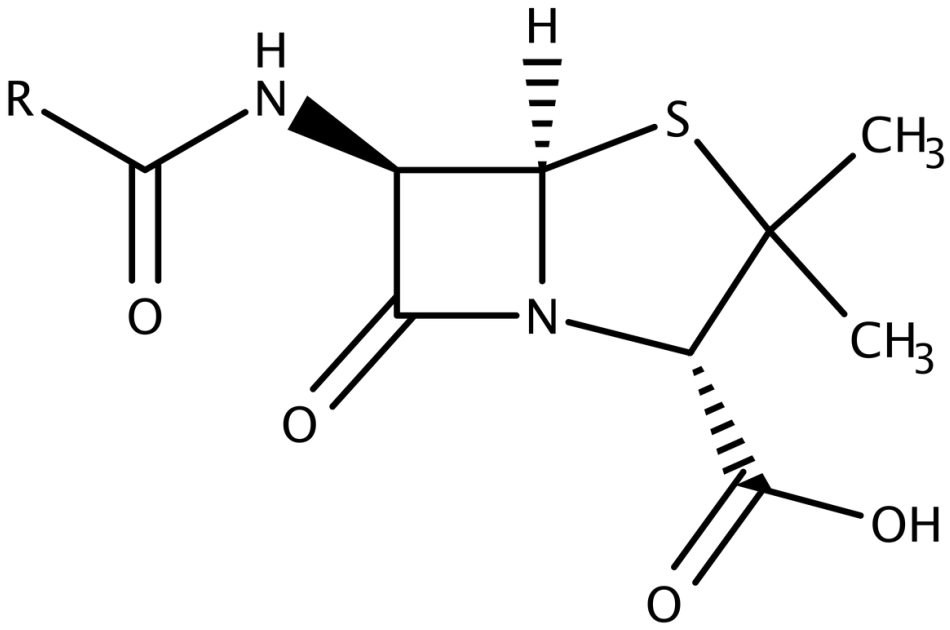
Sir Alexander Fleming

In Oxford, Ernst Chain and Edward Abraham were studying the molecular structure of the antibiotic. Abraham was the first to propose the correct structure of penicillin. Shortly after the team published its first results in 1940, Fleming telephoned Howard Florey, Chain's head of department, to say that he would be visiting within the next few days. When Chain heard that Fleming was coming, he remarked "Good God! I thought he was dead.

Norman Heatley suggested transferring the active ingredient of penicillin back into water by changing its acidity. This produced enough of the drug to begin testing on animals. There were many more people involved in the Oxford team, and at one point the entire Sir William Dunn School of Pathology was involved in its production. After the team had developed a method of purifying penicillin to an effective first stable form in 1940, several clinical trials ensued, and their amazing success inspired the team to develop methods for mass production and mass distribution in 1945. Fleming was modest about his part in the development of penicillin, describing his fame as the "Fleming Myth" and he praised Florey and Chain for transforming the laboratory curiosity into a practical drug.

Fleming was the first to discover the properties of the active substance, giving him the privilege of naming it: penicillin. He also kept, grew, and distributed the original mould for twelve years, and continued until 1940 to try to get help from any chemist who had enough skill to make penicillin. Sir Henry Harris summed up the process in 1998 as: "Without Fleming, no Chain; without Chain, no Florey; without Florey, no Heatley; without Heatley, no penicillin." The discovery of penicillin and its subsequent development as a prescription drug mark the start of modern antibiotics.

Sir Alexander Fleming



Medical use and mass production
In his first clinical trial, Fleming treated his research scholar Stuart Craddock who had developed severe infection of the nasal antrum (sinusitis). The treatment started on 9 January 1929 but without any effect. It probably was due to the fact that the infection was with influenza bacillus (Haemophilus influenzae), the bacterium which he had found unsusceptible to penicillin.

Fleming gave some of his original penicillin samples to his colleague-surgeon Arthur Dickson Wright for clinical test in 1928. Although Wright reportedly said that it "seemed to work satisfactorily", there are no records of its specific use. Cecil George Paine, a pathologist at the Royal Infirmary in Sheffield and former student of Fleming, was the first to use penicillin successfully for medical treatment. He cured eye infections (conjunctivitis) of one adult and three infants (neonatal conjunctivitis) on 25 November 1930

Sir Alexander Fleming

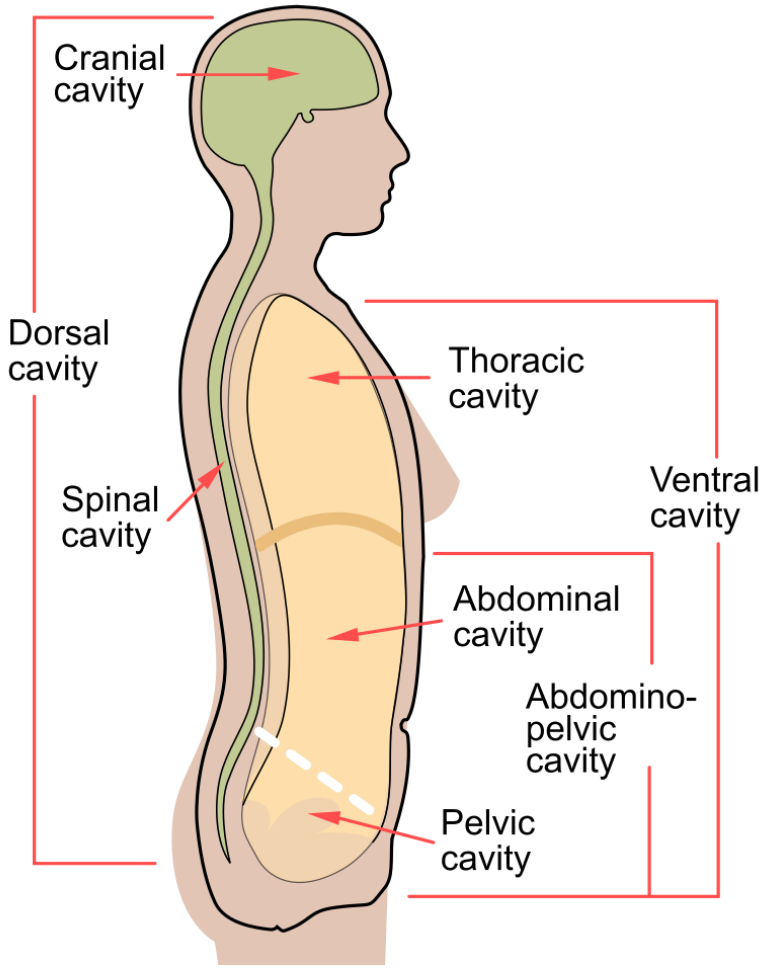
Fleming also successfully treated severe conjunctivitis in 1932. Keith Bernard Rogers, who had joined St Mary's as medical student in 1929, was captain of the London University rifle team and was about to participate in an inter-hospital rifle shooting competition when he developed conjunctivitis. Fleming applied his penicillin and cured Rogers before the competition. It is said that the "penicillin worked and the match was won." However, the report that "Keith was probably the first patient to be treated clinically with penicillin ointment" is no longer true as Paine's medical records showed up.

There is a popular assertion both in popular and scientific literature that Fleming largely abandoned penicillin work in the early 1930s. In his review of André Maurois's The Life of Sir Alexander Fleming, Discoverer of Penicillin, William L. Kissick went so far as to say that "Fleming had abandoned penicillin in 1932... Although the recipient of many honors and the author of much scientific work, Sir Alexander Fleming does not appear to be an ideal subject for a biography." This is false, as Fleming continued to pursue penicillin research. As late as in 1939, Fleming's notebook shows attempts to make better penicillin production using different media. In 1941, he published a method for assessment of penicillin effectiveness. As to the chemical isolation and purification, Howard Florey and Ernst Chain at the Radcliffe Infirmary in Oxford took up the research to mass-produce it, which they achieved with support from World War II military projects under the British and US governments.
By mid-1942, the Oxford team produced the pure penicillin compound as yellow powder. In August 1942, Harry Lambert (an associate of Fleming's brother Robert) was admitted to St Mary's Hospital due to a life-threatening infection of the nervous system (streptococcal meningitis).

Sir Alexander Fleming

Fleming treated him with sulphonamides, but Lambert's condition deteriorated. He tested the antibiotic susceptibility and found that his penicillin could kill the bacteria. He requested Florey for the isolated sample. Florey sent the incompletely purified sample, which Fleming immediately administered into Lambert's spinal canal. Lambert showed signs of improvement the very next day, and completely recovered within a week. Fleming published the clinical case in The Lancet in 1943.

Upon this medical breakthrough, Allison informed the British Ministry of Health of the importance of penicillin and the need for mass production. The War Cabinet was convinced of the usefulness upon which Sir Cecil Weir, Director General of Equipment, called for a meeting on the mode of action on 28 September 1942. The Penicillin Committee was created on 5 April 1943. The committee consisted of Weir as chairman, Fleming, Florey, Sir Percival Hartley, Allison and representatives from pharmaceutical companies as members. The main goals were to produce penicillin rapidly in large quantities with collaboration of American companies, and to supply the drug exclusively for Allied armed forces. By D-Day in 1944, enough penicillin had been produced to treat all the wounded of the Allied troops



Sir Alexander Fleming

Fleming also discovered very early that bacteria developed antibiotic resistance whenever too little penicillin was used or when it was used for too short a period. Almroth Wright had predicted antibiotic resistance even before it was noticed during experiments. Fleming cautioned about the use of penicillin in his many speeches around the world. On 26 June 1945, he made the following cautionary statements: "the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bred out ... In such cases the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted." He cautioned not to use penicillin unless there was a properly diagnosed reason for it to be used, and that if it were used, never to use too little, or for too short a period, since these are the circumstances under which bacterial resistance to antibiotics develops.

It had been experimentally shown in 1942 that S. aureus could develop penicillin resistance under prolonged exposure. Elaborating the possibility of penicillin resistance in clinical conditions in his Nobel Lecture, Fleming said:

The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.

It was around that time that the first clinical case of penicillin resistance was reported.

Sir Alexander Fleming

Personal life

On 24 December 1915, Fleming married a trained nurse, Sarah Marion McElroy of Killala, County Mayo, Ireland. Their only child, Robert Fleming (1924–2015), became a general medical practitioner. After his first wife's death in 1949, Fleming married Amalia Koutsouri-Vourekas, a Greek colleague at St. Mary's, on 9 April 1953; she died in 1986.

Fleming came from a Presbyterian background, while his first wife Sarah was a (lapsed) Roman Catholic. It is said that he was not particularly religious, and their son Robert was later received into the Anglican church, while still reportedly inheriting his two parents' fairly irreligious disposition.

When Fleming learned of Robert D. Coghill and Andrew J. Moyer patenting the method of penicillin production in the United States in 1944, he was furious, and commented:

I found penicillin and have given it free for the benefit of humanity. Why should it become a profit-making monopoly of manufacturers in another country?

From 1921 until his death in 1955, Fleming owned a country home named "The Dhoon" in Barton Mills, Suffolk.

Sir Alexander Fleming

On 11 March 1955, Fleming died at his home in London of a heart attack. His ashes are buried in St Paul's Cathedral.

Awards and legacy

Fleming's discovery of penicillin changed the world of modern medicine by introducing the age of useful antibiotics; penicillin has saved, and is still saving, millions of people around the world.

The laboratory at St Mary's Hospital where Fleming discovered penicillin is home to the Fleming Museum, a popular London attraction. His alma mater, St Mary's Hospital Medical School, merged with Imperial College London in 1988. The Sir Alexander Fleming Building on the South Kensington campus was opened in 1998, where his son Robert and his great-granddaughter Claire were presented to the Queen; it is now one of the main preclinical teaching sites of the Imperial College School of Medicine. His other alma mater, the Royal Polytechnic Institution (now the University of Westminster) has named one of its student halls of residence Alexander Fleming House, which is near to Old Street.

Sir Alexander Fleming (centre) receiving the Nobel prize from King Gustaf V of Sweden (right) in 1945

Sir Alexander Fleming

Sir Alexander Fleming (centre) receiving the Nobel prize from King Gustaf V of Sweden (right) in 1945

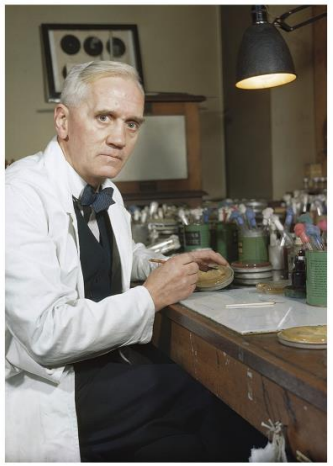
Sir Alexander Fleming

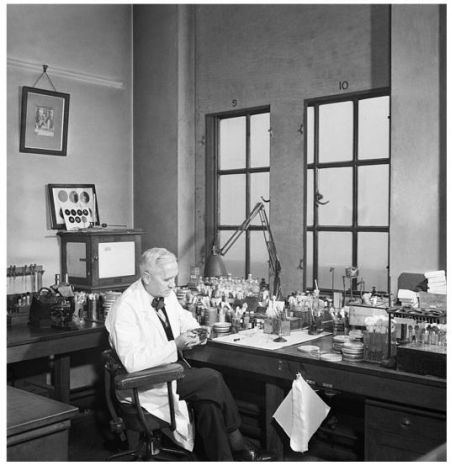
Sir Alexander Fleming (centre) receiving the Nobel prize from King Gustaf V of Sweden (right) in 1945

Sir Alexander Fleming

Fleming, Florey and Chain jointly received the Nobel Prize in Medicine in 1945. According to the rules of the Nobel committee, a maximum of three people may share the prize. Fleming's Nobel Prize medal was acquired by the National Museums of Scotland in 1989 and is on display after the museum re-opened in 2011. He was a member of the Pontifical Academy of Sciences.

He was elected a Fellow of the Royal Society (FRS) in 1943.
He was awarded the Hunterian Professorship by the Royal College of Surgeons of England.
He was knighted as a Knight Bachelor by King George VI in 1944.
He was awarded the Medal for Merit by the President of the United States.
He was made a Grand Cross of the Legion of Honour by the French Republic.
He was made a Grand Cross of the Order of the Phoenix of Greece.
He was made a Knight Grand Cross of the Order of Alfonso X the Wise (Spain) in 1948.
In 1999, Time magazine named Fleming one of the 100 Most Important People of the 20th century

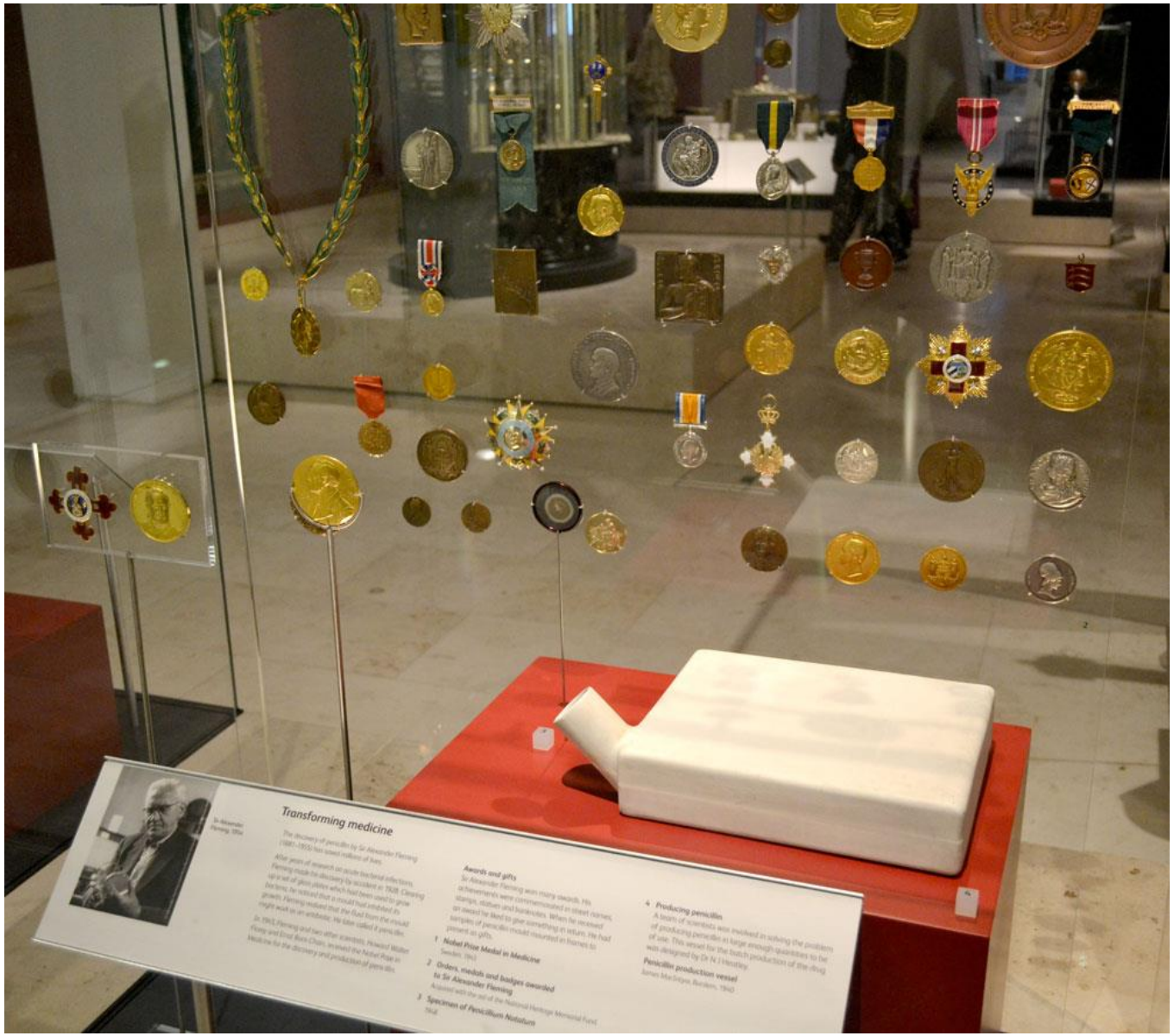




Sir Alexander Fleming

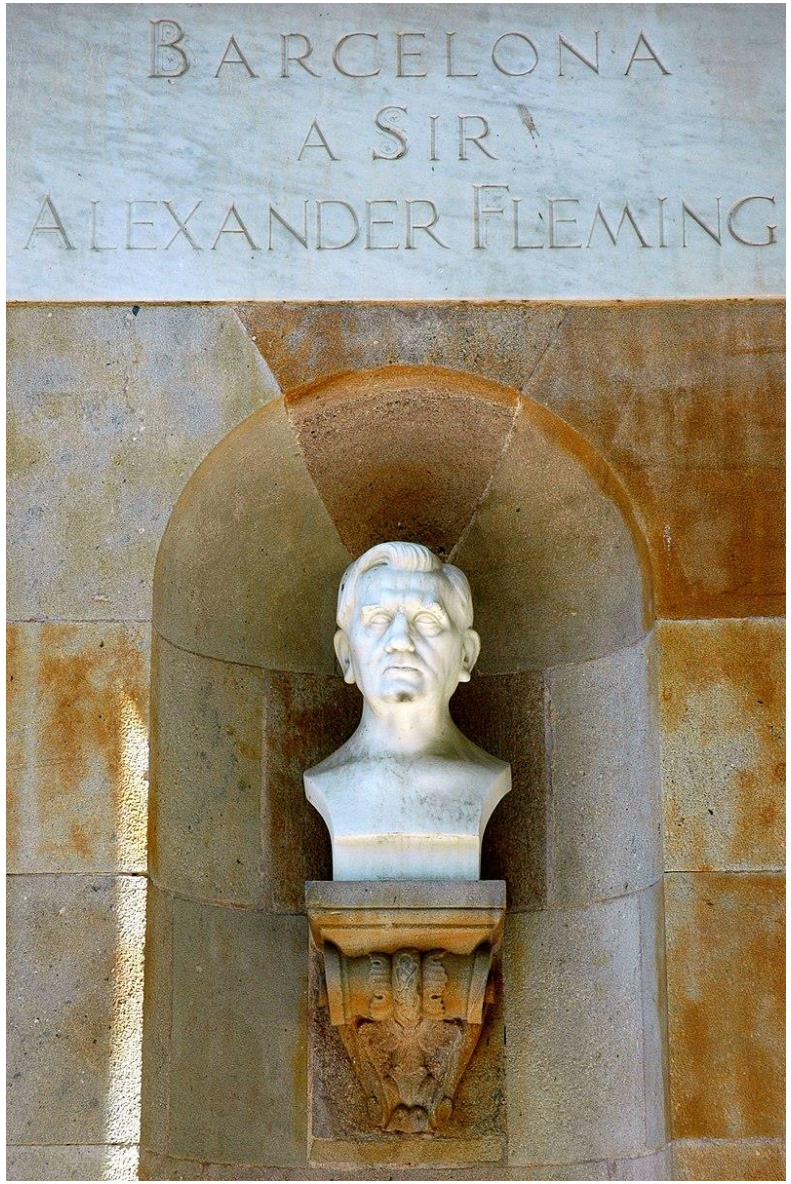
Best known for discovering the world's first broadly effective antibiotic substance, which he named penicillin.

Sir Alexander Fleming



Display of Fleming's awards, including his Nobel Prize. Also shows a sample of penicillin and an example of an early apparatus for preparing it.

Sir Alexander Fleming



Barcelona to Sir Alexander Fleming (1956), by Catalan sculptor Josep Manuel Benedicto. Barcelona: jardins del Doctor Fleming.

Josep Manuel Benedicto.
He was a disciple of Manuel Fuxá, Antonio Alsina and Antonio Parera. In a classicist style, he created various works of public art in Barcelona

To Alexander Fleming (1955), in the Doctor Fleming Gardens, next to the Hospital of the Holy Cross, a marble bust of the discoverer of penicillin, located on a fountain.